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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/613,177	07/10/2000	Kuber T. Sampath	CIBT-P02-540	8978
28120	7590	10/29/2003	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			FREDMAN, JEFFREY NORMAN	
			ART UNIT	PAPER NUMBER

1634

DATE MAILED: 10/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/613,177	SAMPATH ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10, 13, 15, 30-33, 36 and 43-50 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 13, 15, 30-33, 36 and 43-50 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status

Claims 1-10, 13, 15, 30-33 and 36, 43-50 are pending.

Claims 1-10, 13, 15, 30-33 and 36, 43-50 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 10, 2003 has been entered.

Double Patenting

2. Claims 1-10, 13, 15, 30-33 and 36, 43-50 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 5,834,188. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are a species of the genus of the current claims, where the method of claim 2 of the U.S Patent is drawn to a species of screening using OP-1. The species anticipates the genus claim and renders the genus claim obvious.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. The rejection of claims under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Wobus et al (Differentiation (1991) 48:173-182) is withdrawn in view of the amendment.

7. Claims 1, 13, 36, 43, 45, 46, 47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Smart et al (U.S. Patent 5,650,276).

Foulkes teaches a method for identifying a compound that induces a biological effect (column 73, lines 40-43), comprising a) providing a test cell comprising a DNA defining a transcription activating element operatively linked to a reporter gene encoding a detectable gene product, which, when present in a responsive cell contacted with a compound serves to induce transcription of said reporter gene (column 73, lines 44-58), b) exposing said test cell to a candidate compound (column 73, line 59 to column 74, line 5), c) detecting expression of said detectable gene product where the increase in expression of the detectable gene product indicates the ability of the compound to induce the biologic effect (column 73, line 59 to column 74, line 5) and wherein the biological effect requires the presence of the transcription activating element (see, eg. Column 68, lines 10-22, where G-CSF mRNA is increased by the transcription activating element, compounds #542 and #1780). Foulkes expressly teaches producing larger amounts of desirable compounds for use in therapy (column 31).

Foulkes does not teach a motivation to apply the method to morphogenesis or morphogen mediated biological effects in order to identify compounds which induce such effects.

Smart teaches "The invention features a method of screening candidate compounds for the ability to modulate the effective local or systemic concentration or level of morphogenic protein in an organism. (see column 2, lines 61-64)." Smart teaches the desirability of screening candidate compounds for their ability to modulate morphogenic proteins (abstract). Smart expressly teaches OP-1 and OP-2 derived from humans (see column 4, line 38). Smart teaches morphogenic effects such as stimulating proliferation of progenitor cells (See column 2, lines 26-59) including osteoblasts (see column 17, lines 35-36).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Foulkes to the screening of compounds which induce morphogenesis since Smart expressly notes the desirability of screening compounds for their ability to modulate morphogenesis (see column 2, lines 61-64, abstract, column 15, lines 55-64, especially). Further, Foulkes expressly notes that "The present invention provides a method of transcriptionally modulating the expression of a homologous gene-of-interest, the expression of which is associated with a defined physiological or pathological effect within a multicellular organism (see column 22, lines 15-18)". Thus, an ordinary practitioner would have been motivated to apply the method of Foulkes, which studies compounds that are associated with physiological effects to address the morphogenic analysis of Smart. Smart teaches that it is desirable to screen compounds for the physiologic effect of morphogenesis. That is, an ordinary practitioner interested in determining which compounds would effect the physiologic pathway termed morphogenesis as motivated by Smart would have been motivated to

apply the method of Foulkes to this analysis since Foulkes expressly suggests analysis of such pathways and since Foulkes clearly indicates that such screening can result in clinical and therapeutic advantages (see columns 3 and 4, especially column 4, lines 18-28).

8. Claims 1-3, 6, 9, 13, 36, 43-47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Smart et al (U.S. Patent 5,650,276) and further in view of Nadal-Ginard (WO 94/18239).

Foulkes in view of Smart teach the limitations of claims 1, 13, 36, 43, 45, 46, 47 and 49 as discussed above. Smart expressly teaches that OP-1 is associated with cells in the muscle (see column 16, lines 31-33).

Foulkes in view of Smart do not teach the use of the MEF-2 or AP-1 elements, which are functional in muscle cells.

Nadal-Ginard teaches screening for agents which either enhance or decrease the interaction of MEF2 transcription factors as well as MyoD and MASH transcription factors (abstract).

Further, the sequences of Foulkes, Smart or Nadal-Ginard are all "variants" of the nucleotides disclosed in claim 30 and meet this limitation.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Foulkes in view of Smart to the screening of MEF2 related compounds for the study of differentiated tissue as taught by Nadal-Ginard since Nadal-Ginard states "The agents useful in the invention either enhance or decrease the interaction between a pocket protein, eg retinoblastoma

protein and a tissue specific transcription factor, eg members of the MyoD, MEF2 or MASH family of transcription factors" (abstract).⁴ Nadal-Ginard further notes that "Applicant's discovery provides the basis for screening therapeutic agents useful for regulating the switch between the cell's growth phase and a terminally differentiated state (page 4, lines 18-20)". Thus, an ordinary practitioner would have been motivated by Nadal-Ginard to screen for compounds which are involved in differentiation using the MEF2 transcription factor sites in view of Nadal-Ginard's express motivation to use these enzymes in screening between differentiation and growth.

9. Claims 1, 13, 36, 43, and 45-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foulkes et al (U.S. Patent 5,863,733) in view of Smart et al (U.S. Patent 5,650,276) and further in view of Ozkaynak et al (U.S. Patent 5,652,118).

Foulkes in view of Smart teach the limitations of claims 1, 13, 36, 43, 45, 46, 47 and 49 as discussed above.

Foulkes in view of Smart do not teach the association of N-CAM and morphogenesis.

Ozkaynak expressly teaches screening for candidate compounds which alter endogenous morphogen levels (see example 9, column 37-38) and Ozkaynak expressly teaches the association of N-CAM expression with morphogenesis (see column 29).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to apply the method of Foulkes in view of Smart to the screening of N-CAM related compounds since Ozkaynak states "The morphogens described herein induce CAM expression, particularly N-CAM expression, as part of

their induction of morphogenesis (see column 29, lines 2-3)" and since Ozkaynak further states the desirability of compound screening in example 9.

Response to Arguments

10. Applicant's arguments filed September 10, 2003, have been fully considered but they are not persuasive.

Applicant argues that the Foulkes in view of Smart rejection should fall because Foulkes "indirectly" functions like a morphogen while Smart directly acts as a morphogen. Foulkes is directed towards generically detecting compounds of interest by screening for reporter gene activity. Applicant's argument relies upon the theory that a morphogenic compound is distinct from a "morphogen-stimulating compound". This distinction is not found persuasive for several reasons. First, there is no necessary expectation that these compounds would be different, based upon the specification. The specification does not make the distinction which the applicant is now trying to argue. A compound which induces an OP-1 effect will be the same compound, whether it is called a "morphogenic compound" or a "morphogen stimulating compound". Consequently, this argument is simply a linguistic construction which provides no physical difference. Second, there is no distinction in the claim between a "morphogenic compound" or a "morphogen stimulating compound". This means that even if the difference was related to some teaching in the specification which was shown to structurally impact the compounds being screened, the claims lack this element. Third, Smart teaches "The invention features a method of screening candidate compounds for the ability to modulate the effective local or systemic concentration or

level of morphogenic protein in an organism. (see column 2, lines 61-64).” This is an express teaching to screen for morphogenic compounds, where they are simply "morphogenic compound" or are termed "morphogen stimulating compound. Since there is no structural difference between these two elements, the concept of screening a "morphogenic" compound or stimulating compound is taught by Smart.

Applicant relies upon overcoming the prima facie case of Foulkes in view of Smart to overcome the remaining rejections. Since that rejection is maintained, so are the following rejections.

Conclusion

11. This is an RCE of applicant's earlier Application No. 09/613,177. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jeffrey Fredman
Primary Examiner
Art Unit 1634